Matern Child Health J
DOI 10.1007/s10995-014-1651-4

Gestational Diabetes Diagnostic Methods (GD2M) Pilot Randomized Trial

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Abstract To test the feasibility of conducting a pragmatic randomized controlled trial (RCT) comparing the International Association of Diabetes in Pregnancy Study Groups (IADPSG) versus Carpenter–Coustan diagnostic criteria for gestational diabetes (GDM), and to examine patient and provider views on GDM screening. A single-blinded pragmatic pilot RCT. Participants with a singleton pregnancy between 24 and 28 weeks gestation received a 50 g oral glucose challenge test and if the value was <200 mg/dL were randomized to either the 2 h 75 g OGTT using the IADPSG criteria or the 3 h 100 g OGTT using the Carpenter–Coustan criteria. Primary outcome was the feasibility of randomization and screening. Secondary outcomes included patient and provider views (or preferences) on GDM testing. Sixty-eight women were recruited, 48 (71 %) enrolled and 47 (69 %) were randomized. Participants in both study arms identified the main challenges to GDM testing to be: drinking the glucola, fasting prior to testing, waiting to have blood drawn, and multiple venipuntures. Women in both study arms would prefer the 2 h 75 g OGTT or whichever test is recommended by their doctor in a future pregnancy. Physicians and nurse midwives endorsed screening and were comfortable with being blinded to the GDM testing strategy and results values. Both pregnant women and providers value GDM screening, and pregnant women can be recruited to a blinded, randomized GDM screening trial with minimal attrition and missing data.

Keywords Gestational diabetes · Pregnancy · Screening · Randomized clinical trial

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Introduction

Gestational diabetes (GDM) increases risk for obstetrical complications including the birth of a large-for-gestational age (LGA) infant, pre-eclampsia, cesarean delivery, and neonatal morbidity [1–3]. GDM is commonly diagnosed in the United States using a 1-h screening test with a 50-g glucose load followed by a 3-h 100-g glucose tolerance test for those found to have abnormal screening [3]. The approach identifies approximately 5–6 % of the population as having GDM [3]. However, glucose levels lower than those traditionally used for the diagnosis of GDM may also be associated with increased risk for maternal and neonatal morbidity [4]. Based on this knowledge, The International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed a transition to universal testing with a fasting, one-step 75 g oral glucose tolerance test with lower thresholds for the diagnosis of gestational diabetes [5]. The American Diabetes Association endorsed these recommendations in 2011 [6], and the newly recommended diagnostic criteria are expected to increase the prevalence of GDM to approximately 18 % of pregnant women [7].

Any increase in the number of women diagnosed with GDM will incur both societal and personal costs. There are more than 4 million births annually in the United States,

Published online: 26 November 2014

and GDM currently affects approximately 240,000 US women per year. The new diagnostic criteria could potentially increase the number of women with gestational diabetes to 720,000 annually. The National Institutes of Health (NIH) conducted a Consensus Conference in March 2013 and recommended continuing the current two-step approach to GDM diagnosis until additional data are available regarding the risks and benefits of each approach. The decision about how to best screen for GDM will affect a significant proportion of pregnant women, but there are no randomized controlled trials comparing the two screening approaches. We are also lacking qualitative research that assesses patient and provider preferences regarding GDM screening and compliance with testing, which will be an important component of any successful screening strategy. To inform such a trial, we conducted a feasibility study to determine whether randomizing women to either the one-step 2 h 75 g OGTT strategy proposed by the IADPSG or the current two-step screening strategy, using the Carpenter–Coustan criteria, could be done within the context of an efficient and relatively inexpensive comparative effectiveness study. We used a novel effectiveness study design, which enables the examination of the feasibility of randomizing into two screening strategies as well as collecting data on treatment practice and differences in pregnancy and postpartum outcomes within routine clinical practice. We also assessed provider and patient views on and experiences with GDM screening.

Materials and Methods

Trial Design and Setting

We conducted a pilot pragmatic single-blinded randomized controlled trial to test the feasibility and suitability of randomizing pregnant women to one of two strategies for diagnosing gestational diabetes. This trial was conducted at the main clinical laboratory at a large hospital, which provides comprehensive medical services for an ethnically and socioeconomically diverse population of women from southwestern Pennsylvania.

Participants and Selection Criteria

From May 2012 and to February 2013 we recruited women aged 18–45 years with a singleton pregnancy between 18 and 24 weeks' gestation who were receiving prenatal care at an outpatient obstetrical clinic at a large academic teaching hospital. Women were ineligible if they had pre-existing diabetes or a positive screen for diabetes within the first trimester of pregnancy (<24 weeks), multiple gestation, corticosteroid use in the 30 days prior to enrollment, gastric bypass surgery, use of fertility treatments to conceive, plan to deliver at a different hospital, inability to complete the glucose testing before 30 completed weeks GA, or anticipated preterm delivery because of maternal or fetal indications.

Screening Strategy Allocation

The research assistant conducted a prescreening telephone interview to determine eligibility. Participants were then enrolled and scheduled to complete both lab study visits between 24 and 28 weeks of gestation; those participants unable to complete both tests by 30 weeks' gestation were excluded. At the first lab visit after securing written consent, all participants had a non-fasting 1 h 50 g glucose challenge test (GCT) that was consistent with routine clinical care. Participants with glucose values ≥200 mg/dL were considered to have GDM and were not randomized. Their results were unblinded to them and their provider and they were treated as if they had GDM. For participants with glucose values <200, their glucose values were entered into a database that contained the predetermined computer-generated randomization sequence and were randomized into either study arm A: fasting, 2 h 75 g oral glucose tolerance test (OGTT) or study arm B: fasting, 3 h 100 g OGTT (See Fig. 1). Participants returned within 2 weeks after an overnight fast of at least 8 h for a second study visit to complete their OGTT. The research team physician reviewed the lab results and diagnosed GDM using the appropriate criteria. For study arm A, the IADPSG criteria were used, with only one abnormal value required for GDM diagnosis using the following cut-offs: fasting ≥92 mg/dL, 1-h ≥180 mg/dL, and 2-h ≥153 mg/dL; the 50-g GCT result was ignored [5]. Subjects in study arm B were diagnosed with GDM using the Carpenter–Coustan criteria [8] which were a 50-g GCT ≥130 mg/dL and two or more abnormal values on the 3-h OGTT with the following cut-offs: fasting ≥95 mg/dL, 1-h ≥180 mg/dL, 2-h ≥155 mg/dL, and 3-h ≥140 mg/dL. Participants were notified of their GDM status via a phone call and their providers were notified of the diagnosis (GDM, no GDM or did not complete test) via an electronic letter delivered directly to the participants' electronic health record. Treatment for GDM was performed according to clinical care standards of each participant's provider.

Randomization and Blinding

We used computer generated blocked randomization to allocate participants to each of the screening arms in a 1:1 ratio using STATA/SE 12.0 software (StataCorp, College Station, TX, USA). The block size was randomly varied so as to avoid accidental unblinding. *Blinding*-Participants

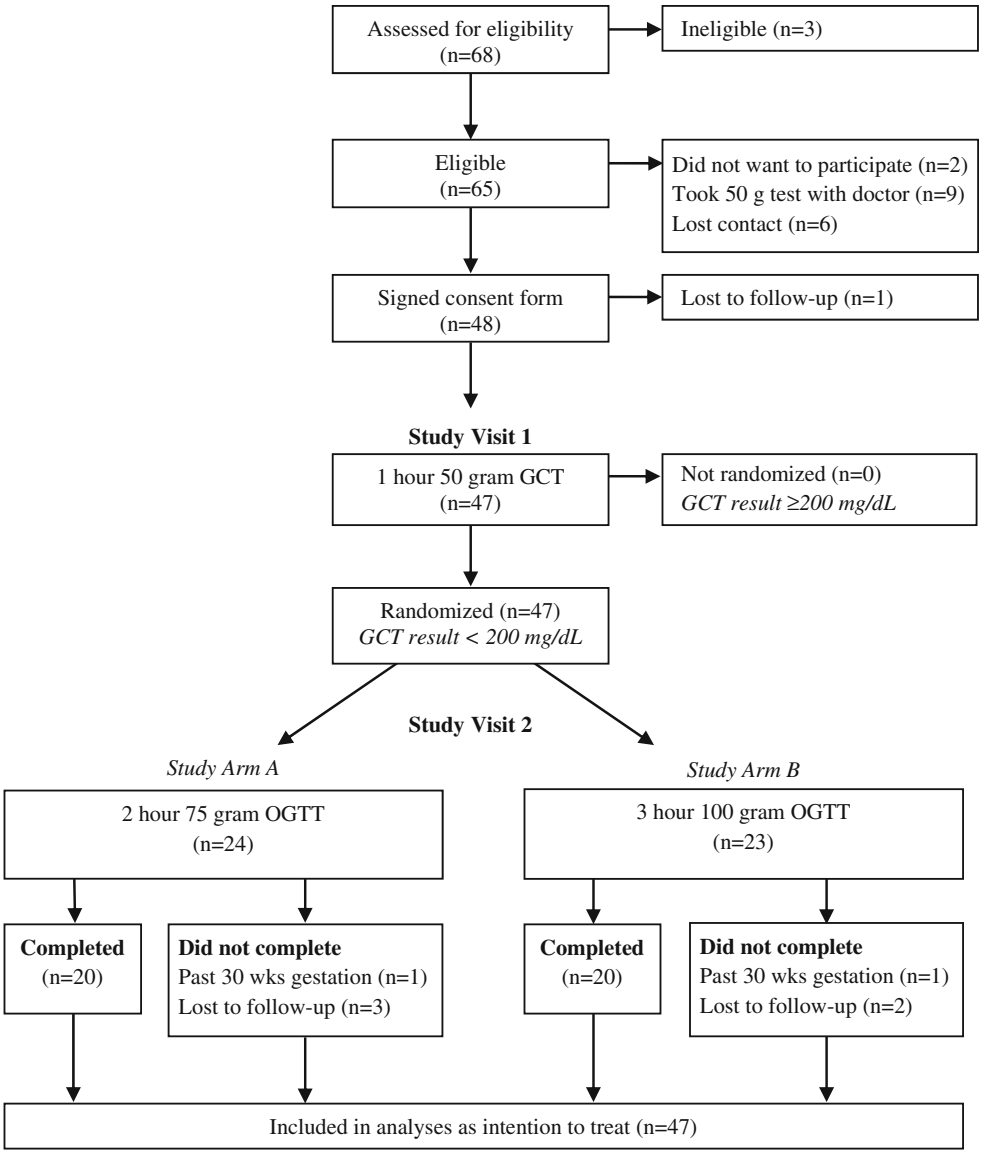

Fig. 1 Selection of participants

were blinded to the specific glucose test they were randomized into until they returned to the lab for the second study visit to have the OGTT test done. Participants were told a priori to be prepared to stay for 4 h for their second study visit to minimize dropout based on knowledge that they were randomized to the longer test and to avoid accidental contamination of the physicians if their prenatal visits occurred prior to the second study lab visit. Providers were blinded to the screening strategy and were notified by the research team physician as to whether or not their patient had GDM, but were not informed of the actual glucose values. Finally, study investigators were blinded to the randomization schema and the study outcomes until completion of the study. Unblinding to the diagnosis, but not the screening strategy, occurred if the participant had a 50 g GCT glucose ≥200, reactive hypoglycemia detected with the 75 g OGTT or 100 g OGTT (blood sugar less than 60 mg/dL with symptoms), inability to complete the 75 g OGTT or 100 g OGTT prior to 30 weeks gestation, or any severe adverse event that warranted immediate medical intervention.

Measurements

Feasibility of Randomization and Ascertainment of Perinatal Outcomes

Primary outcomes included number of participants randomized and the number who completed screening. *Participant views and experiences with GDM testing* were assessed using electronic self-administered questionnaires that participants completed immediately after their 75 and

100 g OGTT. Participants were asked using a Likert scale how difficult it was for them to complete their oral glucose tolerance testing. Participants were also asked what they disliked about the GDM testing and their preference for future testing in another pregnancy. We assessed adverse events between the two study arms and graded them as mild, moderate, or severe.

Provider's views on GDM testing were assessed using an electronic self-administered questionnaire that was sent to providers (obstetricians or nurse midwives) of the practice from which participants were recruited. Because of our modest sample size, it was likely that not all providers who could potentially have patients enroll in a larger study would have patients enrolled in our pilot study. Given our intent to conduct a larger trial, we included all providers whether or not they had patients that participated in this pilot study. The questionnaire measured provider views on the importance of GDM screening and their level of comfort with having their patients randomized to a screening strategy and specific lab values to which they were blinded.

Exploratory outcomes included perinatal outcomes of primary c-section, large for gestational birth weight (defined as birth weight >90th percentile based on US birth weight standards) [9], macrosomia (defined as birth weight ≥4,000 g), and pre-eclampsia (defined as a systolic blood pressure of ≥140 mm Hg or a diastolic blood pressure of ≥90 mm Hg on two occasions at least 6 h apart occurring after 20 weeks gestation accompanied by detectable urinary protein (≥1+ by dipstick or ≥0.3 g/24 h) [10]. We also ascertained type of diabetes treatment, number of diagnostic tests (e.g. ultrasounds, nonstress testing and biophysical profile scoring), and mode of delivery from the electronic medical record.

Main Clinical Variables

Maternal demographic data were abstracted from the medical record including age at delivery, self-reported race/ethnicity (categorized into black/African American, white/Caucasian or other), marital status (included single/never married, divorced, widowed), smoking status (defined as smoking during any trimester, first, second or third trimester, yes/no), and number of prior pregnancies and births. Pre-pregnancy BMI was calculated using height measured at the first prenatal visit and either self-reported pre-pregnancy weight or if missing, the measured weight at the first prenatal visit if participants was less than 12 weeks gestational age (n = 7). These two weight measures were highly correlated, as evidenced by a Pearson correlation coefficient of 0.994 ($p < 0.0001$). Pre-pregnancy BMI category was defined as follows: underweight <18.5 kg/m^2, normal weight 18.5–24.9 kg/m^2, overweight 25–29.9 kg/m^2, obese ≥30 kg/m^2 [11]. Total pregnancy weight gain was calculated using the delivery weight minus the pre-pregnancy weight and grouped into insufficient, appropriate, or excessive based on the 2009 Institute of Medicine recommendations [11].

The study procedures were approved by the Institutional Review Board at the University of Pittsburgh and informed consent was obtained from all patients. This trial was registered at www.clinicaltrials.gov registration NCT01540396.

Statistical Analyses

Each of the outcomes was described using sample means or sample proportions along with 95 % confidence intervals within each study arm. Continuous outcomes were assessed for departures from normality, and suitable transformations were used when needed. Demographic and clinical characteristics were compared between study arms at baseline using either two-sample *t* tests or Chi square test of independence or the appropriate nonparametric counterparts as needed. Any variables that were significantly associated with study arm were included as covariates in primary and secondary analyses.

This study was not powered to detect differences between study arms with respect to perinatal outcomes, but rather was a pilot study to determine feasibility of implementing a study protocol in a real-world practice setting. With an anticipated sample of 40 women, we had a margin of error of no more than 0.15 to estimate the proportion of women randomized and screened. We also sought to obtain patient and provider preferences regarding the two screening strategies. Given the small sample size and exploratory nature of these analyses no corrections for multiple tests were performed such that each was assessed at the 0.05 significance level.

Results

A total of 68 participants were recruited and 48 (71 %) of those enrolled in the study (Fig. 1). Forty-seven women were randomized following completion of the 50 g GCT. There was a 14 % attrition rate with 7 women either withdrawing or being lost to follow-up (Fig. 1), although pregnancy outcomes were obtained on all but one of these women. Maternal demographic and clinical characteristics were similar between the study groups (Table 1).

Table 2 shows the frequency of outcomes by study arms. There was one case (4 %) of GDM diagnosed in the study arm using the IADPSG criteria, and no cases of GDM diagnosed in the study arm using the Carpenter–Coustan criteria, although this finding did not reach statistical significance. The participant diagnosed as having

Table 1 Participant demographic and clinical characteristics at randomization

n (%) or mean ± SD (min, max)	Overall study population (n = 47)	2 h 75 g OGTT (n = 24)	3 h 100 g OGTT (n = 23)	*p* value
Demographic				
Age at consent (years)	25.7 ± 5.9 (18.2, 42.3)	26.1 ± 6.8 (18.2, 42.3)	25.4 ± 5.0 (18.3, 34.6)	0.6826
Race/ethnicity				0.8270
African American	20 (42.6)	9 (37.5)	11 (47.8)	
Caucasian	21 (44.7)	11 (45.8)	10 (43.5)	
Other	3 (6.4)	2 (8.3)	1 (4.3)	
Multiracial[a]	3 (6.4)	2 (8.3)	1 (4.3)	
Marital status: married	14 (29.8)	8 (33.3)	6 (26.1)	0.2786
Education level				0.9930
Less than H.S.	6 (12.8)	3 (12.5)	3 (13.0)	
H.S. diploma/G.E.D	16 (34.0)	8 (33.3)	8 (34.8)	
Some college	16 (34.0)	8 (33.3)	8 (34.8)	
College degree or higher	9 (19.1)	5 (20.8)	4 (17.4)	
Annual household income				0.2128
≤$20,000/year	26 (65.0)	11 (52.4)	15 (78.9)	
$21,000–$40,000/year	7 (17.5)	5 (23.8)	2 (10.5)	
≥$41,000/year	7 (17.5)	5 (23.8)	2 (10.5)	
Clinical characteristics				
Pre-pregnancy BMI (kg/m^2)	26.6 ± 7.7 (17.6, 53.2)	27.3 ± 6.9 (18.8, 42.7)	25.8 ± 8.5 (17.6, 53.2)	0.5232
Pre-pregnancy BMI category				
Underweight (<18.5)	1 (2.2)	0 (0)	1 (4.3)	0.5989
Normal (18.5–24.9)	22 (47.8)	10 (43.5)	12 (52.2)	
Overweight (25–29.9)	10 (21.7)	5 (21.7)	5 (21.7)	
Obese (≥30)	13 (28.3)	8 (34.8)	5 (21.7)	
Weight at 1st prenatal visit (lbs.)	160.1 ± 50.6 (94, 326)	162.8 ± 47.2 (112, 292)	157.3 ± 54.8 (94, 326)	0.7165
Gravidity	3.2 ± 2.5 (1.0, 12.0)	3.3 ± 2.7 (1.0, 12.0)	3.0 ± 2.3 (1.0, 9.00)	0.7365
Parity	1.2 ± 1.4 (0.0, 6.0)	1.3 ± 1.5 (0.0, 6.0)	1.1 ± 1.4 (0.0, 4.0)	0.6327
Gestational weight gain (lbs.)	30.8 ± 18.1 (−4.0, 86.0)	29.2 ± 18.5 (−1.0, 86.0)	32.4 ± 18.1 (−4.0, 68.0)	0.5535
Classification of gestational weight gain				
Insufficient weight gain	9 (19.6)	4 (17.4)	5 (21.7)	0.9185
Appropriate weight gain	17 (37.0)	9 (39.1)	8 (34.8)	
Excessive weight gain	20 (43.5)	10 (43.5)	10(43.5)	
Smoking during pregnancy				
Any trimester	10 (21.3)	6 (25.0)	4 (17.4)	0.5240
First trimester	10 (21.3)	6 (25.0)	4 (17.4)	0.5240
Second and third trimester	5 (10.6)	3 (12.5)	2 (8.7)	0.6724
50 g Glucose challenge test result	98.5 ± 18.0 (66, 142)	98.1 ± 18.6 (66, 142)	99.0 ± 17.7 (70, 134)	0.8759

[a] Multiple race includes Caucasian/Native American, Caucasian/Hispanic, African-American/Native American

GDM by the IADPSG criteria had a fasting value of >92 mg/dL; in reviewing her data post hoc, her initial 50 g screen was 99 mg/dL, which would have classified her as normal under the two-step screening approach. Rates of macrosomia, cesarean delivery, and pregnancy-induced hypertension were also similar between groups.

Patient views and experience with GDM screening are shown in Table 3 for the 41 (85 %) women who completed this information. The majority of participants had discussed GDM testing with their physician or nurse midwife. Most patients reported that the degree of difficulty to complete the fasting OGTT was "not difficult or no trouble at all." Participants in both study arms identified the main challenges to GDM testing as: drinking the glucola, having to fast prior to testing, waiting to have blood drawn, and multiple venipunctures. The latter was the only concern

Table 2 Maternal and neonatal outcomes

	Overall (n = 47) N (%)[a]	2 h 75 g OGTT (n = 24) N (%)[a]	3 h 100 g OGTT (n = 23) N (%)[a]	*p* value
Days between visits 1 and 2 [mean ± SD (min, max)]	14.4 ± 6.8 (5.0, 33.0)	13.9 ± 7.7 (6.0, 33.0)	14.9 ± 6.0 (5.0, 25.0)	0.6493
Gestational age at study visit 2 [mean ± SD (min, max)]	27.3 ± 1.6 (24.0, 30.6)	27.5 ± 1.5 (25.1, 30.6)	27.1 ± 1.7 (24.0, 30.4)	0.4646
Diagnosed with GDM[b]	1 (2.2)	1 (4.3)	0 (0.0)	1.0000 (F)
Patients unblinded to results	6 (12.8)	2 (8.3)	4 (17.4)	0.416 (F)
Gestational age at delivery [mean ± SD (min, max)]	39.4 ± 1.2 (37.0, 42.0)	39.3 ± 1.1 (37.0, 41.0)	39.6 ± 1.3 (37.0, 42.0)	0.4925
Fetal macrosomia	4 (8.7)	1 (4.3)	3 (13.0)	0.2953
Cesarean delivery	4 (8.7)	2 (8.7)	2 (8.7)	1.0000 (F)
Primary cesarean[c]	2 (50.0)	0 (0.0)	2 (100)	
Repeat cesarean[c]	2 (50.0)	2 (100)	0 (0.0)	
Pre-eclampsia	1 (2.2)	1 (4.3)	0 (0.0)	1.0000 (F)
Shoulder dystocia	1 (2.2)	1 (4.3)	0 (0.0)	1.0000 (F)
Birth trauma-3 and 4° vaginal lacerations or postpartum hemorrhage	0 (0.0)	0 (0.0)	0 (0.0)	
Stillbirths	0 (0.0)	0 (0.0)	0 (0.0)	
Number of ultrasounds in 2nd and 3rd trimesters [mean ± SD (min, max)]	1.1 ± 1.7 (0.0, 7.0)	0.9 ± 1.4 (0.0, 5.0)	1.4 ± 2.0 (0.0, 7.0)	0.2691
Number of BPP [mean ± SD (min, max)]	0.4 ± 0.8 (0.0, 4.0)	0.4 ± 0.9 (0.0, 4.0)	0.5 ± 0.8 (0.0, 3.0)	0.8038
Number of imaging/diagnostic tests [mean ± SD (min, max)]	1.6 ± 2.5 (0.0, 9.0)	1.3 ± 2.1 (0.0, 9.0)	2.0 ± 2.8 (0.0, 9.0)	0.3800
Labor induction	10 (22.7)	4 (18.2)	6 (26.1)	0.5237

[a] Unless otherwise noted

[b] 2 h 75 g OGTT group was diagnosed with IADPSG criteria; 3 h 100 g OGTT Carpenter–Coustan criteria

[c] Of those having a cesarean delivery. Percentages were calculated based on women with complete outcome data

that differed by study strategy, with women in the 3 h test more likely to dislike getting stuck by a needle ($p = 0.02$). While there were no significant differences between arms on testing preferences, women in the 2 h, 75 g arm were fairly evenly split between preferring either a one-step or two-step testing paradigm in their next pregnancy, whereas women in the, 3 h 100 g OGTT arm demonstrated preferences for either a one-step test or the test their doctor recommended in their next pregnancy.

Clinicians Views on GDM Screening

The response rate for the electronic survey was 40 % (17 of 42). The providers (physicians and nurse midwives) surveyed were primarily female (94 %), aged 20–29 years (53 %), and physicians (65 %). Of the providers surveyed, 94 % believed screening of all pregnant women for GDM was important, indicated by rating importance of screening of at least 7 on a 1–10 scale. Ninety-two percent of them recommended the current two-step strategy. Among providers with patients in the study most reported being "extremely comfortable/comfortable" with not knowing what testing strategy their patient received (83 %) or with not knowing the specific lab value results (67 %). Among providers who did not have patients enrolled in the study, most (60 %) were extremely comfortable/comfortable with the idea of being blinded to their patients' test results.

Discussion

We have demonstrated that women are willing to participate in a study that examines clinical outcomes based on various screening strategies for gestational diabetes. Our preliminary results also indicate that providers value screening for gestational diabetes, and are willing to have their patients participate in a blinded study to evaluate the efficiency of the two screening methods. The use of the electronic health records enabled us to feasibly recruit and ascertain clinical perinatal outcomes with minimal attrition and missing data.

The willingness of patients and providers to participate in our study is significant because the risks and benefits of screening for mild gestational diabetes are unclear. In a US study assessing the benefits of treatment for mild gestational diabetes there was no difference in the primary

Table 3 Participant experiences with and views on GDM screening

	Overall (n = 47) N (%)	2 h 75 g OGTT (n = 24) N (%)	3 h 100 g OGTT (n = 23) N (%)	*p* value
Spoke to doctor or midwife about GDM screening	31 (75.6)	13 (65.0)	18 (85.7)	0.1936
Degree of difficulty to complete fasting oral glucose tolerance test visit				0.4700
Very difficult or a lot of trouble	1 (2.4)	0 (0.0)	1 (4.8)	
Somewhat difficult or some trouble	10 (24.4)	4 (20.0)	6 (28.6)	
Not difficult or no trouble at all	30 (73.2)	16 (80.0)	14 (66.7)	
Had ≥1 adverse event from testing				
Nausea	7 (14.9)	3 (12.5)	4 (17.4)	0.6378
Diarrhea	1 (2.1)	0 (0.0)	1 (4.3)	0.3018
Fatigue	5 (10.6)	2 (8.3)	3 (13.0)	0.6006
Emesis	1 (2.1)	0 (0.0)	1 (4.3)	0.3018
Dizziness	3 (6.4)	1 (4.2)	2 (8.7)	0.5255
Overall not feeling well	2 (4.3)	2 (8.3)	0 (0.0)	0.1571
Had ≥1 adverse event rated as moderate or severe	1 (2.1)	0 (0.0)	1 (4.3)	0.3018
Dislikes about diabetes testing[a]				
Cost of test	0 (0)	0 (0)	0 (0)	N/A
Taking off from work or school	3 (7.3)	1 (5.0)	2 (9.5)	0.5782
Getting childcare	2 (4.9)	1 (5.0)	1 (4.8)	0.9718
Waiting around to have blood taken	15 (36.6)	7 (35.0)	8 (38.1)	0.8370
Needlestick associated with blood draw	8 (19.5)	1 (5.0)	7 (33.3)	0.0221
				0.0448 (F)
Transportation and/or parking	5 (12.2)	2 (10.0)	3 (14.3)	0.6751
Having to fast for 8 h prior to test	19 (46.3)	9 (45.0)	10 (47.6)	0.8665
Having to drink the sugary drink	17 (41.5)	6 (30.0)	11 (52.4)	0.1459
The testing was fine, no problems at all	11 (26.8)	7 (35.0)	4 (19.0)	0.2492
Preferred method of testing in future pregnancy				0.5669
Current two step (50 ± 100 g)	16 (39.0)	9 (45.0)	7 (33.3)	
One step (2 h 75 g OGTT)	18 (43.9)	9 (45.0)	9 (42.9)	
Do not want any diabetes test	2 (4.9)	1 (5.0)	1 (4.8)	
Test that is recommended by doctor	5 (12.2)	1 (5.0)	4 (19.0)	

[a] Category not mutually exclusive; percentages calculated based on women with complete experience data

outcome which included perinatal mortality or significant morbidity, but there were reductions in the secondary outcomes of pregnancy induced hypertension and macrosomia [12]. In an Australian trial designed to assess treatment of mild GDM there was a reduction in the composite outcome of serious perinatal outcomes such as perinatal death, shoulder dystocia, bone fracture, nerve palsy, and NICU admission [13]. However, this benefit was seen at the cost of an increase in labor induction and higher rates of NICU admission. The number needed to treat for benefit was 34, and the number needed to harm was 11. It is quite plausible that the potential harms associated with the diagnosis of mild gestational diabetes may become more pronounced in a group of women at lower risk of adverse outcomes. Diagnosis of gestational diabetes also leads to multiple interventions during pregnancy, including more frequent prenatal visits, more fetal and maternal surveillance, and interventions such as including induction of labor, late preterm birth, early term birth, and cesarean delivery. It is important to look at these downstream events to ensure that expanding the diagnostic criteria for gestational diabetes results in overall benefits rather than an increase in harms, which is why a larger trial such as we propose is essential to estimate these risks and benefits.

To date current studies have not incorporated the patient perspectives on screening and diagnosis of GDM. Our study provides patient insights to fill this important knowledge gap by identifying the main challenges to GDM testing to be fasting prior to testing, drinking the glucola, multiple venipunctures, and waiting around to have blood drawn. These

patient views are important to consider especially regarding the recommendations to move toward universal testing with a single fasting 2 h OGTT. Currently, the two-step approach has several benefits which include the initial testing to be done in the non-fasting state with only one needle stick for a majority of women, with approximately 14–23 % having to return for the fasting 3 h testing. Interestingly, many women in both arms of the study would prefer a single fasting test in a future pregnancy. However, additional information using qualitative studies are needed to better understand patient preferences [12]. Even the most effective screening program will be ineffective if patient preferences and provider endorsement are not considered. Compliance with testing and tolerability of testing are also important considerations. One study from New Zealand demonstrated a >95 % compliance rate with a 2-h, 75 g OGTT test [14], while other studies have demonstrated that 9.8 % of high-risk women are unable to complete a 3 h, 100 g OGTT [15]. Moving towards universal 2-h 75 g OGTT testing for all pregnant women means that any decrements in the tolerability of testing could have significant implications.

Several limitations deserve a brief mention. We did not directly randomize participants into a "one step" or "two-step" screening strategy. Because the women in the IADPSG arm also received a 50 g GCT, the patient views obtained by survey in our study may not fully represent women's views regarding a one-step test versus two-step test. Our survey allowed patients to report that they would prefer one- or two-step testing, or that they would prefer no testing or the test recommended by their doctor in order to fully assess patient beliefs regarding GDM testing. We used the approach of requiring all women to take the 1 h 50 g GCT test prior to being randomized into either the 2 or 3 h OGTT, because it enabled us to examine the diagnostic abilities of a 50 g GCT in each screening method, and this also ensures blinding of participant providers and investigators to the study arms. However, to compare the one-step to the two-step approaches on outcomes, weignored the results of the 50 g GCT for the one-step arm in the analyses to ensure that the diagnosis of gestational diabetes was made using the same clinical criteria described if one-step testing were adopted into clinical practice. Assessing the efficacy of the 50 g GCT in our study will provide additional clinically relevant information, because the only randomized clinical trial to compare one-step versus two-step screening for the diagnosis of gestational diabetes found that a two-step approach using a 50 g GCT and either a 2-h, 75-g test or a 3 h, 100 g OGTT was less expensive and had equivalent diagnostic power to a one-step approach using the 75 g OGTT [16]. Including the both the 50 g and the OGTTs is an important component of our study design because in a larger trial it would enable the characterization of the number of women with mild glucose intolerance who would have been classified as normal with a two-step approach. Previous studies have not evaluated the ability of the 50 g GCT to detect women who would test positive for GDM on the 2 h OGTT using the IADPSG criteria, and given the improved adherence and cost savings associated with the 50 g GCT [16], this information would help to refine our approach to GDM screening. We used self-reported pre-pregnancy weight and first prenatal weight 12 weeks to calculate pre-pregnancy BMI. Women may have underestimated their pre-pregnancy weight and the first prenatal weight may have overestimated pre-pregnancy weight. However, the Pearson correlation coefficient was 0.995 suggest that there was minimal variation between the self-reported and first prenatal weight.

Despite these limitations, implications and lessons learned from this pilot study that will be informative for the conduction of a larger effectiveness trial include: assessing patient views and willingness to undergo various testing schemes with minimal attrition due to low patient study requirements is one strength of both the current pilot study and a larger study powered to detect differences in clinical outcomes between screening arms. The results of these analyses will be important when translating recommendations from research studies to clinical practice. Blinding is important to assess differences in downstream effects of different testing methods. In clinical practice providers may react differently to GDM diagnosed by more liberal as opposed to more stringent criteria, and it would be difficult to accurately assess the relationship between screening modality and clinical outcomes. The ultimate goal of this work is to provide evidence-based recommendations for the optimal diagnostic methods for gestational diabetes with an adequately powered comparative effectiveness trial.

Conclusions

Pregnant women and their clinicians value GDM screening and are willing to participate in a blinded randomized GDM screening trial.

Acknowledgments This work was supported by funding from Agency for Healthcare Research and Quality Comparative Effectiveness Grant # AHRQ K12 HS019461 and via internal grants/funds received from the University of Pittsburgh Departments of Medicine and Obstetrics, Gynecology, and Reproductive Sciences.

References

1. Hod, M., Merlob, P., Friedman, S., Schoenfeld, A., & Ovadia, J. (1991). Gestational diabetes mellitus: A survey of perinatal complications in the 1980s. *Diabetes, 40*(Suppl 2), 74–78.
2. Yogev, Y., Xenakis, E. M., & Langer, O. (2004). The association between preeclampsia and the severity of gestational diabetes: The impact of glycemic control. *American Journal of Obstetrics and Gynecology, 191*(5), 1655–1660.

3. Practice Bulletin No. 137. (2013). Gestational diabetes mellitus. *Obstetrics and Gynecology, 122*(2 Pt 1), 406–416.
4. Metzger, B. E., Lowe, L. P., Dyer, A. R., Trimble, E. R., Chaovarindr, U., Coustan, D. R., et al. (2008). Hyperglycemia and adverse pregnancy outcomes. *New England Journal of Medicine, 358*(19), 1991–2002.
5. Metzger, B. E., Gabbe, S. G., Persson, B., Buchanan, T. A., Catalano, P. A., Damm, P., et al. (2010). International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. *Diabetes Care, 33*(3), 676–682.
6. Gradmark, A., Pomeroy, J., Renstrom, F., Steiginga, S., Persson, M., Wright, A., et al. (2011). Physical activity, sedentary behaviors, and estimated insulin sensitivity and secretion in pregnant and non-pregnant women. *BMC Pregnancy Childbirth, 11*, 44.
7. Sacks, D. A., Hadden, D. R., Maresh, M., Deerochanawong, C., Dyer, A. R., Metzger, B. E., et al. (2012). Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. *Diabetes Care, 35*(3), 526–528.
8. Carpenter, M. W., & Coustan, D. R. (1982). Criteria for screening tests for gestational diabetes. *American Journal of Obstetrics and Gynecology, 144*(7), 768–773.
9. Alexander, G. R., Himes, J. H., Kaufman, R. B., Mor, J., & Kogan, M. (1996). A United States national reference for fetal growth. *Obstetrics and Gynecology, 87*(2), 163–168.
10. ACOG Practice Bulletin. (2002). Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. *Obstetrics and Gynecology, 99*(1), 159–167.
11. Rasmussen, K. M., Yaktine, A. L., Commitee to Re-examine IOM Pregnancy Weight Guidelines, Institue of Medicine, National Research Council. (2009). *Weight gain during pregnancy: Reexamining the guidelines*. The National Academies Press.
12. Landon, M. B., Spong, C. Y., Thom, E., Carpenter, M. W., Ramin, S. M., Casey, B., et al. (2009). A multicenter, randomized trial of treatment for mild gestational diabetes. *The New England journal of medicine, 361*(14), 1339–1348.
13. Crowther, C. A., Hiller, J. E., Moss, J. R., McPhee, A. J., Jeffries, W. S., & Robinson, J. S. (2005). Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *The New England journal of medicine, 352*(24), 2477–2486.
14. Moses, R. G., Webb, A. J., Comber, C. D., Walton, J. G., Coleman, K. J., Davis, W. S., et al. (2003). Gestational diabetes mellitus: Compliance with testing. *The Australian & New Zealand Journal of Obstetrics & Gynaecology, 43*(6), 469–470.
15. Agarwal, M. M., Punnose, J., & Dhatt, G. S. (2004). Gestational diabetes: Problems associated with the oral glucose tolerance test. *Diabetes Research and Clinical Practice, 63*(1), 73–74.
16. Meltzer, S. J., Snyder, J., Penrod, J. R., Nudi, M., & Morin, L. (2010). Gestational diabetes mellitus screening and diagnosis: A prospective randomised controlled trial comparing costs of one-step and two-step methods. *BJOG: An International Journal of Obstetrics and Gynaecology, 117*(4), 407–415.